REMARKS

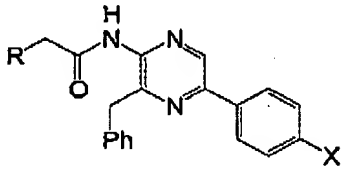
The Applicants appreciate the Examiner's thorough examination of the subject application and request reconsideration of the subject application based on the following remarks.

Claims 3-26, 30, 42-130, 133-146, 154-155, and 162 are pending in the application. Claims 3, 9, and 19 have been amended to cancel non-elected subject matter. Applicants preserve the right to pursue the subject matter of cancelled claims in this or a subsequent application. No new matter has been added by the claim amendments. Support for the amendment to claims can be found in the claims as originally filed and throughout the specification.

Claims 3-8 were rejected under 35 U.S.C. 102(b) as being allegedly anticipated by Hori et al. (Chem. Abstract 80:890, which corresponds to "Bioluminescence of Renilla reniformis. XIII. Identification of the produce excited states during the chemiluminescent and bioluminescent oxidation of Renilla (sea pansy) luciferin and certain of its analogs," *Biochemistry*, (1973), 12(22), 4463-8.

The rejection is traversed.

As the reference is understood, Hori teaches a series of 2-(acetamide)-3-benzyl-5-(*para*-substituted-phenyl)-pyrazine compounds. That is, Hori recites compounds of the formula:



wherein X is hydroxy or methoxy and R is hydrogen or phenyl.

Thus the compounds recited by Hori have a benzyl residue at the R_1 position.

In contrast, compounds provided by claim 3 comprise R_1 H, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, halogen, C_{1-4} haloalkyl, trifluoromethyl, trifluoromethoxy, -NH(C_{1-4} alkyl), -N(C_{1-4} alkyl)(C_{1-4} alkyl), -O(C_{1-4} alkyl), and S(O)$_n$(C_{1-4} alkyl).

Thus compounds provided by claim 3 as presently amended do not comprise those compounds having a benzyl residue at R_1.

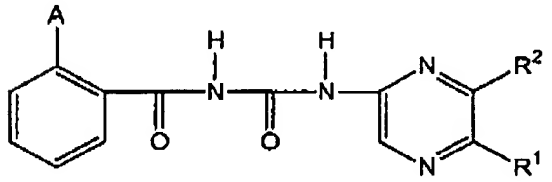
Claim 3 is patentable over Hori. Claims 4-8 depend from claim 3 and are therefore also patentable over Hori.

Claims 9-10 were rejected under 35 U.S.C. 102(b) as being anticipated by Miesel et al. Chem. Abstract 96:35307 (which corresponds to U.S. Patent 4,293,552) and compounds having registry numbers 59489-79-1, 49489-82-6, and 69816-4.

The rejection is traversed.

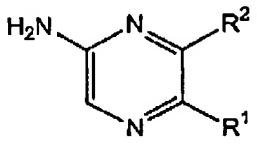
As U.S. Patent 4,293,552 and the CAPlus search printout is understood, Miesel teaches a series of pyrazinyl substituted urea compounds and precursors to making same.

More particularly, Miesel teaches compounds of the general formulae:

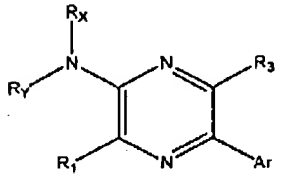


where R^1 may be, among other selections, phenyl or napthyl; and
R^2 is hydrogen, halo, methyl, ethyl, cyano, halomethyl or haloethyl;

Miesel teaches that the above urea compounds are prepared from pyrazine compounds of the formula:



In contrast the claims of the present invention, as amended, provide compounds of the formula:



Formula A

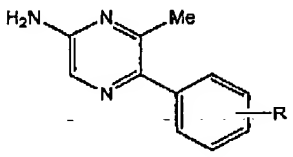
In which $-NH_2$ is excluded from $-NR_XR_Y$. More particularly, R_X and R_Y are defined in claim 9, as follows: R_X and R_Y are the same or different and are independently selected from: hydrogen and straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, each of which alkyl groups may contain one or more double or triple bonds, and may be further substituted with one or more substituent(s) selected from oxo, hydroxy, halogen, $-O(C_{1-4}$ alkyl), $-NH(C_{1-4}$ alkyl), $-N(C_{1-4}$ alkyl)$(C_{1-4}$ alkyl), $-NHC(O)(C_{1-4}$ alkyl), $-N(C_{1-4}$ alkyl)$C(=O)(C_{1-4}$ alkyl), $-NHS(O)_n(C_{1-4}$ alkyl), $-S(O)_n(C_{1-4}$ alkyl), $-S(O)_nNH(C_{1-4}$ alkyl), $-S(O)_nN(C_{1-4}$ alkyl)$(C_{1-4}$ alkyl), Z, and phenyl, optionally mono-, di- or tri-substituted with substituents independently chosen from C1-4 alkoxy, C1-4 alkyl, halogen, CF_3, OCF_3, $OCHF_2$, OH, and CN, **with the proviso that at least one of R_X or R_Y is not hydrogen.**

Compounds of the claimed invention, which have a substituted amino group, e.g., $-NR_XR_Y$ is not $-NH_2$, are not suitable for use as intermediates in the synthesis of the compounds disclosed by Miesel, in part because at least one of the urea nitrogens would be have a non-hydrogen substituent in addition to the pyrazinyl group.

Thus, Miesel neither discloses nor suggests the pyrazinc compounds recited by claim 9. Thus, claim 9 is patentable over Miesel. Claim 10 depends from claim 9 and is therefore also patentable over Miesel.

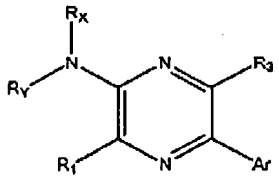
Claims 9 and 10 were rejected under 35 U.S.C. §102(b) as being anticipated by Barnett et al. (U.S. Patent 4,211,870).

As the reference is understood, Barnett teaches in Examples 7, 8, and 9 compounds of the formula:



where R is 3-trifluoromethyl, 4-chloro, or 4-ethyl

In contrast the claims of the present invention, as amended, provide compounds of the formula:



Formula A

In which $-NH_2$ is excluded from $-NR_XR_Y$. More particularly, R_X and R_Y are defined in claim 9, as follows: R_X and R_Y are the same or different and are independently selected from: hydrogen and straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, each of which alkyl groups may contain one or more double or triple bonds, and may be further

substituted with one or more substituent(s) selected from oxo, hydroxy, halogen, -O(C_{1-4} alkyl), -NH(C_{1-4} alkyl), -N(C_{1-4} alkyl)(C_{1-4} alkyl), -NHC(O)(C_{1-4} alkyl), -N(C_{1-4} alkyl)C(=O)(C_{1-4} alkyl), -NHS(O)$_n$(C_{1-4} alkyl), -S(O)$_n$(C_{1-4} alkyl), -S(O)$_n$NH(C_{1-4} alkyl), -S(O)$_n$N(C_{1-4} alkyl)(C_{1-4} alkyl), Z, and phenyl, optionally mono-, di- or tri-substituted with substituents independently chosen from C1-4 alkoxy, C1-4 alkyl, halogen, CF_3, OCF_3, $OCHF_2$, OH, and CN, **with the proviso that at least one of R_X or R_Y is not hydrogen.**

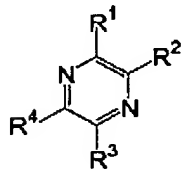
Thus claim 9 is patentable over Barnett. Claim 10 depends from claim 9 and is therefore also patentable over Barnett.

Claims 3-15 were rejected under 35 U.S.C. §103(a) as being allegedly unpatentable over Cox et al. (WO 98/38174).

The rejection is traversed.

Cox teaches a series of *meta*-(substitutedamino)pyrazines having a naphthyl or halogen substituted phenyl or naphthyl group which are therapeutically effective anti-epilepsy agents and which possess sodium channel blockers.

Thus the generic group of compounds recited by Cox comprises compounds of the formula:



wherein

R^1 is selected from the group consisting of phenyl substituted by one or more halogen atoms, naphthyl and naphthyl substituted by one or more halogen atoms;

R^2 is $-NH_2$ or $-NHC(=O)R^a$;

R^3 is $-NR^bR^c$, $-NHC(=O)R^a$ and hydrogen; and
R^4 is hydrogen, C_{1-4}alkyl optionally substituted with halogen, -CN, CH_2OH, CH_2OR^d and $-CH_2S(O)_xR^d$.

Thus, the generic group of compounds embraced by Cox comprises a halogen substituted phenyl and naphthyl optionally substituted with halogen at the R^1 position and an amino ($-NH_2$) or acetamide (-NHC(=O)R) residue at R_2.

Thus, the Cox reference teaches pyrazine compounds in which, as essential features, the compound comprises an amino ($-NH_2$) or an acetamide group *ortho* to a halogen substituted phenyl group or a naphthyl group. Cox neither discloses nor suggests other R^2 substituents *ortho* to the R^1 halophenyl or naphthyl ring. Thus, Cox teaches away from compounds in which the R_2 substituent is modified. That is, Cox teaches away from compounds comprising non-amino or non-acetamido substituents *ortho* to the aryl ring.

In contrast, the compounds of the present invention are outside of the scope of the Cox disclosure, in part because, R^3, as amended, is selected from the group consisting of hydrogen, halogen, C_{1-4} alkyl, $-O(C_{1-4}$ alkyl), $-NH(C_{1-4}$ alkyl), $-N(C_{1-4}$ alkyl)(C_{1-4} alkyl), and $-S(O)_n(C_{1-4}$ alkyl), haloalkyl, trifluoromethyl, trifluoromethoxy, and Y. Thus, R^3 does not encompass amino ($-NH_2$) or acetamide (-NHC(=O)R residues.

Thus, the compounds of claims 3 and 9 are patentable over the teachings and suggestions recited by Cox, in part because the instantly claimed compounds would not have been obvious to one skilled in the art based on the teachings of Cox. Claims 4-8 and 10-15 depend from either claim 3 or claim 9 and are therefore also patentable over the teachings of Cox.

Applicants respectfully request reconsideration of claims 16-26, 30, 42-130, 133-146, 154, 155, and 162. None of the prior art relied upon by the Examiner reads upon any of claims 3-15, as presently amended. As provided by MPEP 803.02, reexamination of the amended

Markush-type claim is proper after the claims have been amended to exclude species of a Markush group which is anticipated or rendered obvious by the prior art.

It is respectfully submitted that the subject application is in a condition for allowance. Early and favorable action is requested.

Applicants believe that additional fees are not required for consideration of the within Amendment. However, if for any reason a fee is required, a fee paid is inadequate or credit is owed for any excess fee paid, you are hereby authorized and requested to charge Deposit Account No. 04-1105.

Respectfully submitted,

Date: December 22, 2003 By: _____

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